REMARKS

Claims 47-50 are pending. Claim 47 has been amended to more particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. Support for the amended claim may be found in the specification, thus, no new matter has been introduced.

A marked up version of the amended claim showing the amendment is attached hereto as Appendix A. Matter that has been deleted is indicated by brackets and matter that has been added is indicated by underlining. A copy of the claims as pending after entry of the foregoing amendment is attached as Appendix B. Applicants respectfully request entry of the amendments and remarks made herein into the file history of the present application.

The Rejections Under 35 U.S.C. § 112, First Paragraph Should Be Withdrawn

Claims 47-50 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors had possession of the claimed invention at the time of filing. Claims 48 and 50 are rejected under 35 U.S.C. § 112, first paragraph because the specification allegedly does not enable a person skilled in the relevant art to make and use the invention commensurate in scope with the claims. Applicants believe these rejections should be withdrawn for the reasons stated below.

The Examiner alleges that the specification fails to adequately describe the genus of compounds to be used in the methods of the invention. This is because no physical or chemical properties of the genus are disclosed. Furthermore, the Examiner contends that one of skill in the art would have no guidance regarding the types of compounds which should be investigated because the specification does not describe how the presence of HBx results in the activation of Src kinase. Applicants contend that the specification has provided a description of the unifying characteristic that distinguishes the members of this genus from others, *i.e.*, the ability to reduce HBx-mediated activation of Src kinase.

The function of the "written description" requirement of 35 U.S.C. 112, first paragraph, is to ensure that Applicants had possession of the claimed subject matter, as of the filing date of application relied on. In re Blaser, 556 F.2d 534, 194 USPQ 122 (CCPA 1977). The inquiry into satisfaction of the written description requirement is factual and depends on

the nature of the invention and the amount of knowledge imparted to those of skill in the art by the disclosure. In re Wertheim, 646 F.2d 527, 191 USPQ 90 (CCPA 1976). Satisfaction of the "written description" requirement does not require *in haec verba* antecedence in the originally filed application. In re Lukach, 440 F.2d 1263, 169 USPQ 795 (CCPA 1971). The written description requirement can be satisfied by showing that the disclosed subject matter, when given its 'necessary and only reasonable construction,' inherently (*i.e.*, necessarily) satisfies the limitation in question. Staehelin v. Secher, 24 USPQ2d, 1513, 1520 (Bd. Pat. Int'f. 1992) ("a specification need not describe the exact details for preparing every species within the genus described"). In general, precedent establishes that although the Applicant 'does not have to describe exactly the subject matter claimed, the description must clearly allow persons of skill in the art to recognize that [the Applicant] invented what is claimed.' In re Gosteli, 872 F.2d 1008,1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989).

To overcome a prima facie case of unpatentability under 35 U.S.C. § 112, first paragraph, Applicants must show by evidence or argument that the invention as claimed is adequately described to one of ordinary skill in the art. In re Alton 76 F.3d 1168, 1175 (Fed. Cir. 1996). The Examiner asserts that the basis of the rejection of the pending claims is that the specification allegedly fails to provide a sufficient description such that members of the genus of inhibitors of HBx-mediated Src kinase activity can be recognized. The specification does in fact provide a sufficient disclosure of the claimed genus to allow one of skill in the art to identify other members of the genus.

According to the Examiner, examples of a precise definition of a genus include the structure, the formula, chemical name, or physical properties. Applicants contend that the cited examples are a *non-exhaustive* list of properties that can be used to sufficiently describe a genus. An Applicant complies with the written description requirement "by describing the invention with all its claimed limitations." Gentry Gallery v. Berkline Corp., 134 F.3d 1473, 1479, 45 USPQ2d 1498, 1503 (Fed.Cir.1998). "One does that by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed.Cir.1997). Rather than limiting the description of a genus to those exact parameters listed by the Examiner, the relevant criteria for written description is that a person of ordinary skill in the art can recognize that the Applicant invented what is claimed. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 1111, 1116 (Fed. Cir. 1991)

(citing In re Gosteli, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989)). "The written description must communicate that which is needed to enable the skilled artisan to make and use the claimed invention." Kennecott Corp. v. Kyocera Int'l, Inc., 835 F.2d 1419, 1421, 5 U.S.P.Q.2d 1194, 1197 (Fed. Cir. 1987), *cert. denied*, 486 U.S. 1008 (1988).

In the present situation, Applicants are not claiming the compounds themselves, but a new use for already existing compounds. Through the use of *in vitro* assays (*see e.g.*, page 38, line 8 to page 40, line 22 and page 42, line 25 to page 43, line 2 of the instant specification) compounds with the desired property (*i.e.*, inhibition of HBx-mediated Src kinase activity) can be identified. The discovery of a new use for an old structure based on unknown properties of the structure might be patentable to the discoverer as a process of using. In re Hack, 245 F.2d 246, 248, 114 USPQ 161 163 (CCPA 1957). One of skill in the art can easily subject candidate compounds to the *in vitro* assays to discern genus members from non-genus members. Using this criteria, *any* compound can be determined to be either inside or outside of the genus.

The Examiner further alleges that one of ordinary skill in the art would have to engage in undue experimentation in order to find the compounds recited in the claims because the specification fails to disclose the signal transduction pathway connecting HBx and Src kinase. Applicants contend that there is no requirement that the mechanism through which the invention works be known. See Exxon Chemical Patents, Inc. v. Lubrizol Corp. 77 F.3d 450 at 456.

> An inventor need not understand the scientific mechanism in order to place an invention into the patent system. See Newman v. Quigg, 877 F.2d 1575, 1581, 11 USPQ2d 1340, 1345 (Fed.Cir.1989) (observing that "it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works"); Fromson v. Advance Offset Plate, Inc., 720 F.2d 1565, 1570, 219 USPQ 1137, 1140 (Fed.Cir.1983) ("[I]t is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests.").

Rather, Applicants have shown that the presence of HBx causes enhanced Src activation (see *e.g.*, Examples 2 and 3 of the instant specification) and this activation is required for HBV replication (see *e.g.*, Example 7 of the instant specification). With this information, one of skill in the art can use the assays described in the specification (*e.g.*, sections 5.5 and 5.5.1) to identify compounds for use in the claimed methods. It is irrelevant what pathway exits between HBx and

Src Kinase - - it is only important to know the desired outcome. Necessarily, any compound that inhibits Src kinase by any mechanism and at any point in the signaling pathway would work in the claimed methods. By defining the cause of the enhanced Src kinase activity as being due to the presence of HBx or HBV in the cell, one would identify those compounds that affect the desired signaling pathway.

Applicants respectfully disagree with the Examiner's position that the scope of the claims is not commensurate with the specification. The Examiner appears to be positing a rule that an Applicant must be limited to claiming only what is present in the working examples. This is not the law. In fact, there is no requirement that an application have any working examples, even when the invention involves a complex technology. See In re Strahilevitz, 668 F.2d 1229, 212 U.S.P.Q. 561 (C.C.P.A. 1982). Therefore, the fact that Applicants have not identified a single compound that inhibits an upstream component of the Src kinase pathway is not material to patentability.

In view of the foregoing, Applicants request that the Examiner withdraws the rejections under 35 U.S.C. §112, first paragraph.

The Rejection Under 35 U.S.C. § 102 Should Be Withdrawn

Claims 47-50 are rejected under 35 U.S.C. § 102(b) as being anticipated by Moriya et al., 1996, *Biochem Biophys. Res. Commun.* 218:217-223 ("Moriya"). The Examiner alleges that Moriya teaches the inhibition of HBV by administration of HBx antisense oligonucleotides. As such, the Examiner contends that the inherent properties of the oligonucleotides would encompass the claimed subject matter. Applicants respectfully disagree.

Moriya teaches the administration of HBx antisense oligonucleotides to HBx-expressing transgenic mice. Experiments were done in an effort to probe the connection between HBx expression and hepatocellular carcinoma pathogenesis (a condition to which the mice are predisposed). Because Moriya never infects the mice with HBV, the sole source of HBx is the recombinantly engineered transgene. Expression levels of transgenic HBx are assayed both in the presence and absence of the antisense oligonucleotides and a correlation is alleged between decreased HBx expression levels and a decrease in preneoplastic lesions in the liver.

The Examiner alleges that, because the oligonucleotides were shown to decrease HBx expression, they would necessarily also decrease HBx-mediated Src kinase activation, and thus inherently have the properties of the compounds recited in the claims. Applicants believe

that this assertion is error. There is no indication that the reduced expression levels of HBx indeed have an affect on Src kinase activation - - Moriya did not contemplate assaying such a parameter. Furthermore, the reduced HBx expression was assayed in a system expressing only one HBV protein. There is no indication that HBx expression would be similarly decreased in a virally-infected cell expressing all of the HBV proteins. Assuming *in arguendo* that the decreased HBx expression levels did impact the level of HBx-mediated Src kinase activation in a HBV-infected cell, there is no indication that this reduced activation would inhibit HBV replication. The threshold at which HBV cannot replicate for lack of Src kinase activity is unappreciated by Moriya as are *in vitro* assays to determine if such a level has been reached. Using the system disclosed in Moriya, one could never know if the oligonucleotides were inhibiting HBV replication because viral infection is never done.

In order for a reference to anticipate a claim, each and every element of the claim must be disclosed in that one reference. Orthokinetics, Inc. v. Safety Travel Chairs, Inc., 1 U.S.P.Q.2d 1081 (Fed. Cir. 1985). "Anticipation under Section 102 can be found only if a reference shows exactly what is claimed. . . ." Structural Rubber Prod. Co. v. Park Rubber Co., U.S.P.Q. 1264 (Fed. Cir. 1984). If it is necessary to reach beyond the boundaries of a single reference to provide a missing disclosure of the claimed invention, it is not a § 102 anticipation. Scripps Clinic & Research FDN. v. Genentech Inc., 927 F.2d 1565, 18 USPQ2d 1869 (Fed. Cir. 1991). Furthermore, anticipation is not shown even if the differences between the claims and the prior art reference are argued to be "insubstantial" and the missing elements could be supplied by the knowledge of one skilled in the art. Structural Rubber Prod. Co. v. Park Rubber Co., 221 USPQ 1264 (Fed. Cir. 1984). Moreover, in Jamesbury Corp. v. Litton Industrial Products, Inc., 225 USPQ 253 (Fed. Cir. 1985), the Court stated that the assertion of invalidity for lack of novelty, if the prior art disclosed "substantially the same thing", is erroneous. The prior art must meet each claim limitation in order to constitute an anticipation under § 102.

If the prior art reference does not expressly set forth a particular element of the claim, that reference still may anticipate if that element is "inherent" in its disclosure. To establish inherency, the extrinsic evidence "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." Continental Can Co. v. Monsanto Co., 948 F.2d 1264, 1268, 20 U.S.P.Q.2d 1746, 1749 (Fed. Cir.1991). "Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of

circumstances is not sufficient." Id. at 1269, 948 F.2d 1264, 20 U.S.P.Q.2d at 1749 (quoting In re Oelrich, 666 F.2d 578, 581, 212 U.S.P.Q. 323, 326 (C.C.P.A.1981)).

In view of the foregoing, Applicants request that the Examiner withdraws the rejection under 35 U.S.C. §102.

CONCLUSION

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the present application. Withdrawal of the Examiner's rejections and a notice of allowance are earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

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APPENDIX A
MARKED VERSION OF THE AMENDED CLAIM
U.S. PATENT APPLICATION SERIAL NO. 09/096,589
ATTORNEY DOCKET NO. 5914-065-999

47. A method for inhibiting Hepatitis B virus (HBV) replication comprising administering a compound to an HBV-infected patient that inhibits enhanced activity of Src kinase wherein said enhanced activity results from the presence of HBx.

APPENDIX B
PENDING CLAIMS AS OF JULY 29, 2002
U.S. PATENT APPLICATION SERIAL NO. 09/096,589
ATTORNEY DOCKET NO. 5914-065-999

47. (amended) A method for inhibiting Hepatitis B virus (HBV) replication comprising administering a compound to an HBV-infected patient that inhibits enhanced activity of Src kinase wherein said enhanced activity results from the presence of HBx.

48. A method for inhibiting Hepatitis B virus (HBV) replication in a cell wherein Src kinase activity is enhanced comprising administering a compound that reduces the enhanced activation of Src kinase activity to levels comparable to those observed in the absence of HBV.

49. The method of Claim 47 or 48 wherein the compound that inhibits said enhanced activity of Src kinase is determined by an *in vitro* assay comprising:

a) contacting a cell expressing HBx with the compound;

b) determining whether levels of Src kinase activity are reduced in those cells contacted with the compound as compared to levels of Src kinase activity in cells expressing HBx in the absence of the compound.

50. The method of claim 47 or 48 wherein said compound inhibits a Src kinase signaling cascade component other than Src kinase as determined by an *in vitro* assay comprising:

a) contacting a Src kinase with said compound; and

b) determining whether levels of Src kinase activity in the presence of said compound are substantially equal to levels of Src kinase activity in the absence of said compound.